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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/773,374	02/01/2001	Bing-Yan Zhu	021390-001820US	4008

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EXAMINER
TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
1624	22

DATE MAILED: 09/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/773,374	ZHU ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5-8 and 11* is/are allowed.

6)☒ Claim(s) *9 and 12-16* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment of 7-7-03 has been considered. Although the amended claims 5 and 10 have overcome the previous rejection of 112/2nd, it is noted that claim 9 has a proviso that is not related to the chemical structure. It is also noted that claim 15 recites a method of treating many diseases that are related to factors other than thrombosis, and thus, a rejection of "scope of enablement" is presented herein. .Also, in reviewing the references of record, the teaching of **Hirayama et. al.** bears relevant subject matter, and prompts the following 103 rejection.

Because new grounds of rejection presented, the FINALITY of the previous action is withdrawn herein.

Claims 1-4 have been cancelled, leaving claims 5-16 remaining for consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 recites the proviso, which seems irrelevant to formula IV because said formula does not have variables E and J. Thus, it is unclear what compounds are excluded from claim 9.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of thrombosis or embolism, related diseases, post coronary angioplasty, etc., does not reasonably provide enablement for preventing said diseases, or procedure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The quantity of experimentation necessary;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The breadth of the claims;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The quantity of experimentation necessary: Many of the diseases recited in claim 15 relates to factors other than thrombosis. For example, acute coronary syndrome, myocardial infarction, transient ischemic attack (TIA) are associated with angiogenesis, lipid, cholesterol, hypertension, etc. Likewise, angina and cerebrovascular syndrome are caused by factors such as lipid, cholesterol, arteriosclerosis, etc. Thus, it would take more than an antithrombotic agent to prevent said diseases.

The amount of direction or guidance presented: While the specification provides the assay for antithrombotic effect, it does not provide data that can substantiates preventing thrombosis and related diseases or procedures. There is no guidance for administering the claimed compounds in terms of the 'on set' and the duration of 'prevention'.

The state of the art: The state of the art, as evidence by the teaching of **Hirayama** (WO 99/37643), discloses quinolinone compounds for the treatment of thrombosis or embolism, but does not provide evidence for the prevention of said diseases, or related procedures.

The relative skill of those in the art: Even if one skilled in the art knows how to treat acute coronary disease, angina, TIA, etc., one would have to do more than routine experiment to select an effective compound for preventing said diseases or procedures.

The predictability or unpredictability of the art: The pharmaceutical art has always been an unpredictable art. A compound effective for thrombosis alone does not necessarily mean it can prevent said diseases. Note, in order to prevent, one would have to know when to administer the drug, and when to discontinue the drug. "Prevention" usually has a short

duration, and does not require repeating dosage (e.g., vaccine). In the instant case, the claimed compounds do not meet the requirement of prevention.

The breadth of the claims: The breadth of claims 14 and 15 recite the prevention of a plethora of diseases using compounds of formulae III-V, and quinolinone. Such a scope embraces not only the prevention, but also the compounds. With a myriad of compounds claimed herein, and the limited guidance provided, the enablement for such a scope has not been met adequately.

For the reasons set forth above, the prevention of all diseases in claims 14 and 15 would require undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 12-14, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Hirayama et. al.** (WO 99/37643 – cited on IDS). On page 33, Table 4 lists compound #16 which is analogous to a compound of tetrahydro-quinolinone recited in claim 12 with the following substituents:

i. A-Z represents CH_3-C-(=NH)-(*N*-piperidinyl);

ii. E-J-G represents $-(CH_2)_2$-phenyl-C(=NH)NH_2.

The disclosed compound is also used as an antithrombotic agent. However, it differs from the claimed compound by not having a dihydro-quinolinone ring, and not having a saturated alkylene chain corresponding to –E-J. Said difference can be overcome by the equivalent teaching provided for the genus of the disclosed formula (I). The definition of Y in said genus allows for lower alkylene (which would give a *tetrahydro-quinolinone*) as well as –CR^7=CH- (which would give a *dihydro-quinolinone*). Likewise, the definition of A in said genus allows for –CH=CR^4-CH_2 as well as –CH_2-CH_2-CH_2-. With such an equivalent teaching, one of the ordinary skill in the art would have been motivated to make a compound of substituted dihydro-quinolinone as claimed herein because one would have expected the claimed compound to treat thrombosis as well.

Thus at the time of the invention, it would have been obvious to one skilled in the art to make and use a compound of the claimed substituted dihydro-quinolinone in view of the teaching of Hirayama et. al.

Claim Objections

4. Claim 10 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

5. Claims 5-8, and 11 allowed.

6. The following is a statement of reasons for the indication of allowable subject matter:

The prior arts of record do not teach compounds of quinoxalinone with substituents as claimed herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (5:00-12:30) & every Saturday morning (starting from 4-7-03).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
***
September 12, 2003

Alan L Rotman

ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
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